UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,426	06/26/2007	Carsten Hopf	50125/114001	8157

21559 7590 12/01/2009

CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER	
GUCKER, STEPHEN	
ART UNIT	PAPER NUMBER
1649	

NOTIFICATION DATE	DELIVERY MODE
12/01/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/587,426	HOPF ET AL	
	Examiner	Art Unit	
	STEPHEN GUCKER	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *1-6,11 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 July 2009* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/22/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

1. Applicant's election without traverse of Group VII, claims 7-10, in the reply filed on 10/27/09 is acknowledged. The Examiner would like to thank the attorney for indicating that the assignment of claim 6 to Group VII was indeed in error as it properly should belong in Groups I-VI as noted. The Examiner apologizes for any confusion this may have caused.

2. Claims 1-6 and 11-12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10/2709.

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. §1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §1.821-1.825 for the reason(s) set forth below: The disclosure contains sequences which fall under the purview of 37 CFR 1.821 through 1.825 as requiring SEQ ID NOs., but none are provided. For example, see Figures 2 and 3. Also see the nucleotide sequences on pages 18 and 46.

Applicant must fully comply with the sequence rules for any response to this action to be considered fully responsive.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed invention is directed to a method of identifying a gamma-secretase and/or a beta-secretase modulator comprising the step of a) identifying a ATP7A-interacting molecule by determining whether a given test compound is a ATP7A-interacting molecule, and b) determining whether the ATP7A-interacting molecule of step a) is capable of modulating gamma-secretase and/or beta-secretase activity. At issue for the purpose of written description is the lack of adequate written description for the genus of ATP7A molecules possessing the biological activity of interacting with one or more components of the gamma-secretase and/or beta-secretase complex, such that a molecule that binds to ATP7A is both an inhibitor of ATP7A activity and a modulator, e.g. agonist or antagonist, of gamma-secretase and/or beta-secretase activity that affects the ability of APP to be cleaved.

> *Vas-cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification should "clearly allow persons of ordinary skill in the art to recognize that (he or she) invented what is claimed." (See *Vas-cath* at page 1116).
>
> The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (see *In re Shokal* 113USPQ283(CCPA1957); *Purdue Pharma L.P. vs Faulding Inc*. 56 USPQ2nd 1481 (CAFC 2000).
>
> To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their

complete structure. A species of copper-transporting ATPases (ATP7A) is known in the art to be part of the Psen2 complex and of the BACE1-complex, which are known to regulate directly or indirectly the activity of gamma-secretase (page 3). ATP7A is a ubiquitously expressed (except for liver) P-type copper-transporting ATPase comprising 8 transmembrane segments and 6 N-terminal metal binding domains. Defects in ATP7A are associated with Menkes disease (MD) and occipital horn syndrome (OHS) in humans, probably due to a defect in absorption and transport of copper (page 4). However, the specification discloses that the term "ATP7A" does not only mean the protein as shown in Figure 2, but also a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant encoded by a nucleic acid that hybridizes to the nucleic acid encoding ATP7A, and the specification does not disclose the portion(s) of wildtype ATP7A that are responsible for manifesting the interaction between ATP7A and members of the gamma-secretase and/or beta-secretase complex so as to affect gamma-secretase and/or beta-secretase activity upon the cleavage of APP as postulated. Thus, the method embraces the use of an enormous genus of structurally undisclosed variants of ATP7A/ATP7A-like polypeptides that not necessarily possess the desired biological activity of interacting with one or more members of the gamma-secretase and/or beta-secretase complex.

The Revised Interim Guidelines state:

> "The claimed invention as a whole may not be adequately described if the claims require an essential or critical element which is not adequately described in the specification and which is not conventional in the art" (col. 3, page 71434), "when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus", "in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus" (col. 2, page 71436).

> An Applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).
>
> Possession may also be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the Applicant was in possession of the claimed invention. See, e.g., *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 1 19 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998), *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997)*, *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it").

Therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. See *Fiers v. Revel*, 25 USPQ2d 1602 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. *In Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Without a correlation between structure and function, the claim does little more than define the claimed invention by function. That is not sufficient to satisfy the written description requirement. *See Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406 (“definition by function … does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is”).

Applicant has not provided any description or reduction to practice of a method for identifying a gamma-secretase and/or beta-secretase modulator comprising the step of identifying a ATP7A-interacting molecule by determining whether the given test compound binds to ATP7A and modulates gamma-secretase and/or beta-secretase activity to cleave APP. Based on the Applicant's specification, the skilled artisan cannot envision the detailed chemical structure of the enormous genus of ATP7A and variants thereof that are capable of enhancing or suppressing the activity of gamma-secretase and/or beta-secretase to cleave APP when bound to a structurally undisclosed compound that binds to and inhibit at least one ATP7A activity, as encompassed by the claims.

The inventive concept is Applicant's apparent discovery that siRNAs directed against the species ATP7A, but not a siRNA directed against unrelated Luc3 specifically reduces ATP7A-mRNA in SK-N-BE2 neuroblastoma cells over-expressing APP695 *in vitro* (page 48 and Figure 1B). No adequate description is provided of an interaction between a genus of ATP7A variants and members of the gamma-secretase and/or beta-secretase complex or of ATP7A-interacting molecules that are capable of modulating gamma-secretase and/or beta-secretase activity. Thus, the artisan is dependent upon Applicant's disclosure to reveal that domain or domains of ATP7A (the species) responsible for modulating gamma-secretase and/or beta-secretase activity, as measured by APP cleavage, for example, and relating it back to the genus of ATP7A as defined by Applicant's disclosure.

Accordingly, given that the specification does not describe what are the domains of the species of ATP7A shown in Figure 2 that bestows upon ATP7A its desired biological properties of interacting with an ATP7A-interacting molecule, and then said interacting-molecule would

further modulate gamma-secretase and/or beta-secretase activity as required by the claim language, it is deemed that the specification is insufficient to reasonably convey to one skilled in the art that Applicant is in possession of the required starting materials, that is functional variants or derivatives of ATP7A, to perform the necessary active steps and effect the claimed method, at the time the application was filed.

Thus, for the reasons outlined above, it is concluded that the claims do not meet the requirements for written description under 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 7-10 are indefinite because the term, "ATP7A" is not clearly defined. Since abbreviations often have more than one meaning, it is suggested that inserting the full name of the transmembrane protein or providing it with a SEQ ID NO would overcome the instant rejection.

Claims 7-10 are also indefinite because while the preamble of claim 7 recites, "a method for identifying a gamma-secretase and/or a beta secretase modulator", the methods steps conclude with "determining whether the ATP7A-interacting molecule of step a) is capable of modulating gamma-secretase and/or beta-secretase activity". There is not a clear nexus

between the purpose of the claim as stated in the preamble and the last method step. Thus, it is unclear how the method steps accomplish the purpose of the claim as stated in the preamble. Furthermore, there are no clear active process steps which set forth how a ATP7A-interacting molecule is identified (see step a of claim 7), or how modulation of secretase activity is determined (step b). Bringing the test compound into contact with ATP7A does not set forth how the interaction with the test compound is determined (claim 8) or what ATP7A activity should be measured for inhibition (claim 9). Claim 10 is also indefinite for the clause beginning with “preferably” because it is unclear what limitation is intended with the use of the word “preferably".

6. No claims are allowable.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Gucker whose telephone number is 571-272-0883. The examiner can normally be reached on Mondays through Fridays from 0930 to 1800.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen Gucker

November 27, 2009

/Jeffrey Stucker/

Supervisory Patent Examiner, Art Unit 1649